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EXAMINER	
JUNG, UNSU	
ART UNIT	**PAPER NUMBER**
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/797,813	CRUM, ALBERT	
	Examiner	Art Unit	
	Unsu Jung	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-62* is/are pending in the application.

4a) Of the above claim(s) *21-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-62* is/are rejected.

7)☒ Claim(s) *51,52,55-58 and 60* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment to cancel claims 1-20 and add claims 37-62 has been acknowledged and entered.

2. Claims 21-62 are pending.

Election/Restrictions

3. Applicant's election with traverse of Group II (originally claims 7-13) in the reply filed on December 5, 2005 is acknowledged. The traversal is on the ground(s) that claims define a single invention and that all of the claims should be examined in this application. Applicant further argues that the claims define methods of testing for lipid peroxide, pyroglutamic acid and glutathione and comparing the amounts of these compounds before, during and after treatment with an anti-oxidant. This is not found persuasive because each method of Groups I-IX and XI has a distinct step, which is not required by the others as discussed in Office Action filed on August 5, 2005.

The requirement is still deemed proper and is therefore made FINAL.

4. In the Office Action dated June 29, 2005, the Group XI claims only included claim 33, which was a typographical error. The Group XI should have included claims 33-36.

5. As a result of addition of new claims 37-62 in the reply filed on December 5, 2005, further restriction to one of the following inventions is required under 35 U.S.C. 121:

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 37-44, drawn to a method for assessing the need for treatment of a subject with an anti-oxidant, classified in class 424, subclass 94.1, for example.

II. Claims 45-62, drawn to a method for measuring the effectiveness of therapy with an anti-oxidant in a subject receiving treatment with an anti-oxidant, classified in class 424, subclass 94.2, for example.

III. Claim 21, drawn to a method for determining the amount of IMMUNE FORMULATION 100™ or IMMUNE FORMULATION 200™, which is necessary to increase glutathione synthesis or re-synthesis in a patient in need of such therapy, classified in class 424, subclass 278.1, for example.

IV. Claim 22, drawn to a method for determining the amount of IMMUNE FORMULATION 100™ or IMMUNE FORMULATION 200™, which is necessary to reduce urine pyroglutamic acid in a patient in need of such therapy, classified in class 514, subclass 2, for example.

V. Claim 23, drawn to a method for determining the amount of IMMUNE FORMULATION 100™ or IMMUNE FORMULATION 200™ that is necessary to reduce urine lipid peroxide in a patient in need of such therapy, classified in class 562, subclass 575, for example.

VI. Claim 24, drawn to a method for determining an orally anti-oxidative effective amount of IMMUNE FORMULATION 100™ or IMMUNE FORMULATION 200™ sufficient to diminish urine lipid peroxide and pyroglutamic acid levels and concurrently increase blood plasma glutathione levels, classified in class 424, subclass 279.1, for example.

VII. Claim 25, drawn to a method for establishing the interdependence of lipid peroxides, pyroglutamic acid, glutathione, and immune cell number and/or function in a subject suffering from oxidative stress, classified in class 562, subclass 573, for example.

VIII. Claim 26, drawn to a method for determining and immune enhancing effective amount of IMMUNE FORMULATION 100™ or IMMUNE FORMULATION 200™ sufficient to normalize CD4+, CD8+ T cell numbers and natural killer cell activity in a subject suspected of experiencing oxidative stress, classified in class 424, subclass 283.1, for example.

IX. Claims 27 and 28, drawn to a method for determining an orally anti-oxidative effective amount and an immune enhancing effective amount of IMMUNE FORMULATION 100™ or IMMUNE FORMULATION 200™ sufficient to normalize lipid peroxides, pyroglutamic acid and glutathione levels in a subject suspect of experiencing oxidative stress, wherein the normalization of lipid peroxides, pyroglutamic acid and glutathione levels results in immune enhancement, classified in class 424, subclass 280.1, for example.

X. Claim 29-32, drawn to a kit for measuring oxidative stress in a subject, classified in class 435, subclass 7.1, for example.

XI. Claims 33-36, drawn to a method for providing a course of therapy for an individual suspected or know to be suffering from oxidative stress, classified in class 424, subclass 184.1, for example.

6. The inventions are distinct, each from the other because of the following reasons:

7. Inventions I-IX and XI are independent and patentably distinct. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the method of Group I includes a step of determining that the levels of lipid peroxide and pyroglutamic acid in a sample of body fluid from a subject suspected of needing anti-oxidative treatment and glutathione in blood plasma outside the normal range are indicative of a need for anti-oxidant treatment, which is not required by the methods of Groups II-IX and XI. The method of Group II includes a step of determining that the presence of normal levels of lipid peroxide and pyroglutamic acid in a sample of body fluid from a subject being treated with anti-oxidative and blood plasma glutathione are an indication of effectiveness of the anti-oxidant therapy, which is not required by the methods of Groups I, III-IX, and XI. The method of Group III includes a step of determining that the presence of normal levels of lipid peroxide and pyroglutamic acid in a sample of body fluid from a subject

being treated with anti-oxidative and blood plasma glutathione are an indication of efficiency of utilization of the anti-oxidant, which is not required by the methods of Groups I, II, IV-IX, and XI. The method of Group IV includes correlating normalization of lipid peroxide and pyroglutamic acid levels in body fluid samples with the synthesis or re-synthesis of glutathione in the patients receiving IMMUNE FORMULATION 100™ or IMMUNE FORMULATION 200™, which is not required by the methods of Groups I-III, V-IX, and XI. The method of Group V includes correlating reductions of pyroglutamic acid to normal levels in body fluid samples with the amount of IMMUNE FORMULATION 100™ or IMMUNE FORMULATION 200™ sufficient to achieve a beneficial effect, which is not required by the methods of Groups I-IV, VI-IX, and XI. The method of Group VI includes determining whether a decrease in lipid peroxide and pyroglutamic acid levels correlates with an increase in glutathione levels and the correlation establishes an orally anti-oxidative effective amount of IMMUNE FORMULATION 100™ or IMMUNE FORMULATION 200™, which is not required by the methods of Groups I-V, VII-IX, and XI. The method of Group VII includes measuring the number of CD4+ and CD8+ T cells and the natural killer cell activity from the cellular component of whole blood obtained from a subject suspected of being under oxidative stress and providing support for the interdependence of the level of oxidative stress in the subject and immune cell number and/or function, which are not required by the methods of Groups I-VI, VIII, IX, and XI. The method of Group VIII includes correlating between the does of IMMUNE FORMULATION 100™ or IMMUNE FORMULATION 200™ that is sufficient to normalize CD4+, CD8+ T cell numbers and natural killer cell

activity establishes an immune enhancing effective amount of IMMUNE FORMULATION 100™ or IMMUNE FORMULATION 200™, which is not required by the methods of Groups I-VII, IX, and XI. The method of Group IX includes determining whether a decrease in urinary lipid peroxide and pyroglutamic acid levels correlates with an increase in glutathione levels, and whether the normalization of the levels of all threes of these products relates to a normalization of CD4+ and CD8+ T cells numbers and normalization of natural killer cell activity, which is not required by the methods of Groups I-VIII and XI. The method of Group XI includes determining the identity and levels of at least three markers of oxidative stress in a sample of body fluid from individuals suspected or known to be suffering from oxidative stress and selecting the appropriate course of therapy for the individual, which are not required by the methods of Groups I-IX. Therefore, the methods of Groups I-IX and XI have different modes of operation, function and effects.

8. Inventions X and I-IX, XI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the product as claimed can be used in a materially different process. For example, the product of Group X can be used in methods of Groups I-IX and XI.

9. Because these inventions are distinct for the reasons given above, have acquired a separate status in the art because of their recognized divergent subject matter, and searches for one group are not required for the others, restriction for examination purposes as indicated is proper.

10. During a telephone conversation with Ms. Cord on December 28, 2005 a provisional election was made with traverse to prosecute the invention of Group II, claims 45-65. Affirmation of this election must be made by applicant in replying to this Office action. Claims 21-41 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

11. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Specification

12. The abstract of the disclosure is objected to because a comma in line 8 following the phrase "needed for" should be deleted. Correction is required. See MPEP § 608.01(b).

13. The use of the trademarks IMMUNE FORMULATION 100™ (pp5-12, 15, 18, 19, 24, 25, 30-32, 37, 39, 48, 51-53, 63-65, and 69), IMMUNE FORMULATION 200™ (pp5-

12, 15, 18, 19, 24, 25, 30-32, 37, 39, 48, 51, 54, 63-65, 70, and 71), BIOXYTECH® (p37, paragraph [0110], line 1 and paragraph [0113], line 1)), AMSCOT™ (p37, paragraph [0112], line 2), and IMMUNE FORMULATION™ (p40) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

14. Claims 51, 52, and 56-58 are objected to because of the following informalities: the word "anti-oxidant" should be corrected to "anti-oxidant" to be consistent with the rest of the claims. Appropriate correction is required.

15. Claims 52 and 57 are objected to because of the following informalities: a comma is needed following the word "glycine" in line 3. Appropriate correction is required.

16. Claim 55 is objected to because of the following informalities: a comma is needed following the words "subject" in line 5 and "standard" in lines 14 and 17. Appropriate correction is required.

17. Claim 60 is objected to because of the following informalities: a comma is needed following the word "standard" in lines 3 and 5. Appropriate correction is required.

Claim Rejections - 35 USC § 112

18. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

19. Claims 51 and 56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The subject matter of a composition comprising a whey product containing from about 65% to about 85% protein, which is from about 65% to about 100% denatured" is not described in the current specification. The current specification discloses "protein, which is from about 65% to 100% **undenatured**" on p18.

20. Claims 55 and 60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The subject matter of comparing the level of blood plasma glutathione with that of a standard, wherein when the amount of lipid peroxide and pyroglutamic acid in the sample and the level of blood plasma glutathione are outside the standard, there is a need for anti-oxidant treatment and wherein when the amount of lipid peroxide and pyroglutamic acid in the sample and the level of blood plasma glutathione in the sample are within the standard, it is an indication of the effectiveness of the treatment with the anti-oxidant was not described in the current specification.

21. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

22. Claims 45-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

23. Claim 45 recites the limitation "the effectiveness" in line 1. There is insufficient antecedent basis for this limitation in the claim.

24. In claim 45, the term “an anti-oxidant” in lines 2 and 4-5 is vague and indefinite. It is unclear whether or not the term “an anti-oxidant” is referring to “an anti-oxidant” in lines 1-2.

25. In claim 45, the term “a subject” in line 4 is vague and indefinite. It is unclear whether or not the term “a subject” is referring to “a subject” in line 2.

26. Claim 45 recites the limitation "the amount" in line 6. There is insufficient antecedent basis for this limitation in the claim.

27. Claim 45 recites the limitation "the level" in line 7. There is insufficient antecedent basis for this limitation in the claim.

28. Claim 45 recites the limitation "the presence" in lines 12 and 13. There is insufficient antecedent basis for this limitation in the claim.

29. In claim 46, the term “an anti-oxidant” in line 2 is vague and indefinite. It is unclear whether or not the term “an anti-oxidant” is referring to “an anti-oxidant” in lines 1-2 of claim 45.

30. In claims 46 and 47, the term "therapy" in line 3 is vague and indefinite. It is unclear whether or not the term "therapy" is referring to "anti-oxidant therapy" in line 14 of claim 45.

31. Claim 48 recites the limitation "the group" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. It is suggested that Applicant change the phrase "the group" to "a group."

32. Claim 49 recites the limitation "the group" in line 1. There is insufficient antecedent basis for this limitation in the claim. It is suggested that Applicant change the phrase "the group" to "a group."

33. Regarding claim 50, the use of parentheses renders the claim indefinite because it is unclear whether the limitation(s) within the parentheses are part of the claimed invention.

34. Claims 50 and 58 contain the trademark/trade names IMMUNE FORMULATION 100™ and IMMUNE FORMULATION 200™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material

or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe anti-oxidant and, accordingly, the identification/description is indefinite.

35. In claims 51 and 56, the phrase "from about 5% to about 95% by weight of the composition of a whey product containing from about 65% to about 85% protein, which is from about 65% to about 100% denatured and from about 5% to about 95% by weight of the composition of colostrums" in lines 3-6 is vague and indefinite. The phrase contains numerous grammatical errors and generally fails to clearly define the composition of the anti-oxidant. For the purpose of examination, the phrase is interpreted in light of the current specification on p18, which defines a composition containing a catalytic quantity of elemental selenium or a water soluble selenium precursor; from about 5% to about 95% of a special whey product containing from about 65% to about 85% protein, which is from about 65% to about 100% undenatured; and from about 5% to about 95% by weight of colostrums.

36. The term "about" in claims 51 and 56 is a relative term which renders the claims indefinite. The term "about" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The weight

compositions of the whey product, the protein, and the colostrums have been rendered indefinite by the use of the term "about."

37. Claim 55 recites the limitation "the need" in line 1. There is insufficient antecedent basis for this limitation in the claim.

38. Claim 55 recites the limitation "the effectiveness" in line 2. There is insufficient antecedent basis for this limitation in the claim.

39. In claim 55, the term "a subject" in lines 4 and 5 is vague and indefinite. It is unclear whether or not the term "a subject" is referring to "a subject" in lines 1.

40. In claim 45, the term "an anti-oxidant" in lines 5 and 6 is vague and indefinite. It is unclear whether or not the term "an anti-oxidant" is referring to "an anti-oxidant" in lines 1-2.

41. Claim 55 recites the limitation "the amount" in line 7. There is insufficient antecedent basis for this limitation in the claim.

42. Claim 55 recites the limitation "the level" in line 9. There is insufficient antecedent basis for this limitation in the claim.

43. Claims 61 and 62 recite the limitation "the group" in line 2. There is insufficient antecedent basis for this limitation in the claim. It is suggested that Applicant change the phrase "the group" to "a group."

Claim Rejections - 35 USC § 103

44. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

45. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

46. Claims 45, 53, 55, and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gillam (WO 01/89518 A1, Nov. 29, 2001) in view of Crawford (U.S. Patent No. 6,709,835, Filed Sept. 3, 1996) and Ajami (U.S. Patent No. 6,284,219, Filed June 30, 1998).

Gillam teaches a method of determining a dosage of anti-oxidant for an individual person, wherein the dosage is determined on the basis of an individual factor and a stress index (Abstract). Anti-oxidants are chemical molecules present in small amounts in the body that can accept an electron from an oxygen radical, thus deactivating it, and preventing oxidative damage (p1, lines 18-20). The body produces its own anti-oxidants, the most important of which is glutathione (GSH, p1, lines 20-21). When the number of oxygen free radicals within the body increase beyond the amount of anti-oxidants in the body, the body is said to be under "oxidative stress" (p2, lines 9-10). These oxygen radicals rapidly react with fats, proteins and DNA, damaging their molecular structure, which can cause abnormal metabolic and cellular functions, disruptions in cell structure, leakage of essential enzymes involved in energy production and genetic damage that may lead to the development of chronic diseases, such as cancer (p2, lines 9-14). The levels of plasma GSH progressively decrease from 25 to 45 years of age to 50% of their original level (p6, lines 1-2). As a consequence, the concentration of lipid peroxides, an index of oxidative damage to lipid, rises with increased age (p6, lines 2-4). It would be obvious to one of ordinary skill in the art to realize that the measurements of reduced levels of plasma GSH and increased lipid peroxide in aging individuals would require comparison between an aging group of individuals and a control group (normal standard). However, Gillam fails to teach a method measuring the amount of pyroglutamic acid levels in a sample of body fluid and that lipid peroxide levels were measured in a sample of body fluid.

Crawford teaches a method of measuring by products of free radical damage such as lipid peroxide and glutathione, which can be an indicator for oxidative stress, in serum or urine (column 2, lines 4-8 and lines 24-34). Crawford further teaches that glutathione is a well known cellular anti-oxidant and its function as powerful anti-oxidant is essential for cell-mediated immune functions (column 2, lines 13-20). Research in humans has indicated that deficient intakes of nutrient anti-oxidants are associated with higher risks of cancer, cardiovascular disease, arthritis, cataracts, etc. (column 1, lines 60-62). Also, a higher intake of nutrient anti-oxidants is associated with lower incidence of chronic degenerative diseases (column 1, lines 62-64). Encouraging studies indicate that intervention with anti-oxidant nutrient supplements may have therapeutic benefit in humans (column 1, lines 64-67).

Ajami teaches that the measurement of cytoprotective capacity and resistance to oxidative stress, as reflected in the glutathione cycle, is immediately applicable in cancer treatment to assess a given patient's ability to withstand a dose of chemotherapy (column 15, lines 58-52). Patients with AIDS, hepatitis, and long term neurodegenerative disorders, such as Parkinson's and Alzheimer's disease might also benefit (column 15, lines 55-57). Ajami further teaches that the level of oxoproline (pyroglutamic acid, PGA), a natural substrate of oxoprolinase, is inversely proportional to the level of glutathione as oxoproline accumulates in toxic concentrations when glutathione synthesis is inhibited (column 16, lines 59-66) and oxoproline level is decreased during periods of high glutathione demand (column 16, line 59-column 17, line 5). Moreover, Ajami teaches a method of comparing between a metabolic index

value obtained for the patient and the normative value for the control population. This method can be used as a tool in the selection of gradations in therapy and track a course of therapeutic treatment (column 16, lines 22-28).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Gillam with a method of measuring urine of serum level of lipid peroxide as taught by Crawford and a method of measuring PGA levels as taught by Ajami in order to assess oxidative stress levels, determine effective anti-oxidant therapy as glutathione, lipid peroxide, and PGA are indicators of oxidative stress in an individual, and track a course of therapeutic treatment.

With respect to claims 53 and 59, Ajami teaches a method, wherein the sample is urine (column 14, lines 5-8).

With respect to claim 54, Ajami teaches a method, wherein comparison of metabolic index value (lipid peroxide, PGA, and glutathione levels) of a patient to a normal individual is used to track a course of a therapeutic treatment (an indication of efficiency of utilization of anti-oxidant, column 16, lines 22-28).

47. Claims 46-49 and 60-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gillam (WO 01/89518 A1, Nov. 29, 2001) in view of Crawford (U.S. Patent No. 6,709,835, Filed Sept. 3, 1996) and Ajami (U.S. Patent No. 6,284,219, Filed June 30, 1998) as applied to claims 45 and 55 above, and further in view of Khaled (U.S. Patent No. 5,977,073, Filed June 6, 1991).

Gillam in view of Crawford and Ajami teaches a method for measuring

effectiveness of therapy with anti-oxidant in a subject receiving treatment with an anti-oxidant as discussed above. However, Gillam in view of Crawford and Ajami fails to teach a method, wherein the subject in need of treatment with an anti-oxidant also experiences a reduction in immune cell number and/or function.

Khaled teaches that an immune system can be compromised because of poor dietary habits or starvation, various environmental stresses that include physical, psychological, infection, trauma, ischemia, radiation, chemical exposure, cigarette, alcohol, or narcotic substance abuse, and the toxic effect of one or more therapeutic drugs (column 1, line 62-column 2, line 1). A paradigm of such stress is found in AIDS, which appears to involve several nutritional aberrations (column 2, lines 1-2). HIV is a T-cell lymphotropic retrovirus that severely infects T-helper cells, and causes severe malnutrition (column 2, lines 2-4). Such malnutrition increases the susceptibility of the patient to opportunistic diseases that form the basis of AIDS or AIDS related complex (column 2, lines 4-7). Among deficient nutrients in AIDS patients, or in HIV-infected patients, are anti-oxidants (column 2, lines 7-8). These immune disorders, which are caused by a virus and/or bacterium, can be treated by using antiviral and/or antibacterial pharmacological agents together with a nutritional supplement, which both bolsters the immune competence of the patient and reduces the toxicity of the antiviral and/or antibacterial agent.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Gillam in view of Crawford and Ajami to include treating AIDS patients, or in HIV-infected patients, whose T-helper cells ($CD4^+$ T

cells) are severely infected resulting in severe malnutrition, with anti-oxidants as taught by Khaled in order to bolster the immune competence of the patient and reduce the toxicity of the antiviral and/or antibacterial agent.

48. Claims 50, 51, 56, and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gillam (WO 01/89518 A1, Nov. 29, 2001) in view of Crawford (U.S. Patent No. 6,709,835, Filed Sept. 3, 1996) and Ajami (U.S. Patent No. 6,284,219, Filed June 30, 1998) as applied to claims 45 and 55 above, and further in view of Crum (WO 99/64022 A1, Dec. 16, 1999).

Gillam in view of Crawford and Ajami teaches a method for measuring effectiveness of therapy with anti-oxidant in a subject receiving treatment with an anti-oxidant as discussed above. However, Gillam in view of Crawford and Ajami fails to teach a method, wherein the anti-oxidant comprises a formulation consisting of a glutathione precursor, which is IMMUNE FORMULATION 100™ or IMMUNE FORMULATION 200™. For the purpose of examination, the IMMUNE FORMULATION 100™ or IMMUNE FORMULATION 200™ are interpreted in light of the current specification as defined on pp52-53.

Crum teaches a nutritional composition containing selenium (0.01-50g), colostrums (0.01-100g) and whey (0.01-100g) for enhancement of immune system and glutathione levels (p13, lines 17-25 and p31). Crum teaches that dietary supplement of selenium has been shown to provide a protective effect in cells against peroxidase (p13, lines 2-5).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Gillam in view of Crawford and Ajami with a nutritional composition of Crum containing selenium (0.01-50g), colostrums (0.01-100g) and whey (0.01-100g) in order to enhance of immune system and glutathione levels in an individual.

With respect to claims 51 and 56, Crum teaches a composition containing selenium (0.01-50g), colostrums (0.01-100g) and whey (0.01-100g) for enhancement of immune system and glutathione levels (p13, lines 17-25 and p31), wherein whey product contains substantially undenatured proteins (80%, p21, lines 4-11).

49. Claims 52 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gillam (WO 01/89518 A1, Nov. 29, 2001) in view of Crawford (U.S. Patent No. 6,709,835, Filed Sept. 3, 1996) and Ajami (U.S. Patent No. 6,284,219, Filed June 30, 1998) as applied to claims 45 and 55 above, and further in view of Yegorova (U.S. PG Pub. No. US 2002/0176900 A1, Filed Nov. 22, 2000).

Gillam in view of Crawford and Ajami teaches a method for measuring effectiveness of therapy with anti-oxidant in a subject receiving treatment with an anti-oxidant as discussed above. However, Gillam in view of Crawford and Ajami fails to teach a method, wherein the anti-oxidant comprises a formulation comprising a catalytic quantity of selenium source together with a mixture of glutamic acid, cysteine or cysteine precursor, and glycine, wherein the glutamic acid:cysteine or cysteine precursor:glycine ratio is 1:0.5:1. For the purpose of examination, the catalytic quantity

of selenium source is interpreted in light of the current specification. The catalytic quantity of selenium precursor is defined by the current specification on p55, paragraph [0169] as an amount necessary to produce either in one dosage unit or in multiple dosage units sufficient elemental selenium to promote the production and activation of glutathione.

Yegorova teaches a composition comprising a catalytic quantity of selenium, cysteine, glutamic acid and glycine (p3, paragraphs [0015] and [0016]). Cysteine, glutamic acid and glycine form glutathione, an anti-oxidant important in many enzyme systems (p6, paragraph [0053], lines 1-9). Anti-oxidants made from glutathione and selenium protect cells against oxidative stress (p6, paragraph [0053], lines 9-12). Yegorova discloses the claimed composition except for glutamic acid, cysteine or cysteine precursor, and glycine having a ratio of 1:0.5:1, respectively. It would have been obvious to one having ordinary skill in the art at the time the invention was made to determine the optimal ratio of glutamic acid, cysteine or cysteine precursor, and glycine, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include in the method of Gillam in view of Crawford and Ajami with a composition of Yegorova comprising a catalytic quantity of selenium and three amino acids, cysteine, glutamic acid and glycine, which comprise a glutathione, in order to enhance glutathione levels in an individual to protect cells against oxidative stress.

Conclusion

50. No claim is allowed.

51. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Unsu Jung whose telephone number is 571-272-8506. The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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